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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,370	10/03/2001	Randall K. Holmes	33,383-00	8568

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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,370	Holmes et al	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,3,4,6-8,11,13-17,28,29, 30,32-34,37 and 39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2,4,6-8,11,13-17,28,30,32-34,37 and 39-43* is/are rejected.

7)☒ Claim(s) *3, 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11, 13-17, 28-37,39-43 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 12, 2004 has been entered.

Response to Arguments

2. Applicant's arguments with respect to claims 1-2, 4-11, 13-17, 28, 30-37, 39-43 have been considered but are moot in view of the new ground(s) of rejection.

Allowable Subject Matter

3. Claims 3, 29 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claims 1-2, 4, 6-8,11, 13-17, 28, 30,32-34, 37, 39-43 are rejected under 35 U.S.C. 102(b) as being anticipated by WO95/17211 (as evidenced by sequence for cholera toxin and E.coli heat labile enterotoxin provided by Zhang et al (1995, page 564, Figure 1)).

WO95/17211 disclose a mutant (see abstract, claims 4-5) cholera holotoxin (see page 6, lines 20-21), wherein the mutation is a deletion mutation at position 7 (see claim 4), which would result in a substitution of tyrosine at position 29 (see evidence provided by Zhang et al showing tyrosine at position 30, which would become position 29, upon deletion of position 7).

The mutant cholera toxin which evidences a deletion at position 7 is disclosed to be a detoxified mutant with adjuvant activity and is combined with a second antigen (see WO95', page 6, lines 34-38; page 7, lines 25-28; page 8, lines 7-27; page 9, lines 2-11).

The compositions of WO95' comprise an antigen or antigens (see page 9, line 36). The antigens disclosed include bacterial, viral, protozoan, allergens, allogens, tumour and self antigens (see page 9, lines 2-11), wherein specific vial antigens that include HSV gD

glycoprotein (see page 9, lines 20-24), Helicobacter pylori (see page 9, line 24), meningococcus A, B and C (see page 8, lines 26-27), respiratory virus (RSV, see page 8, line 21) are disclosed. The reference discloses the administration of the whole, attenuated or inactivated organism which inherently comprise the recited pathogen associated antigens (see page 9, lines 10-11), such as H.pylori urease, Neisseria meningitides (meningococcus) porA or rpilin, Herpes simplex virus glycoprotein D2, RSV.

The mutant cholera holotoxin, antigen or antigens are combined with a diluent or carrier (see page 9, lines 36-38; and pages 10-11, specifically page 11, lines 15-19).

The compositions are also disclosed to comprise two adjuvants, one being the mutant cholera holotoxin and the second being any one of a number of adjuvants listed on pages 10-11 (also see page 12, lines 15-16).

An additional mutation disclosed in combination with the tyrosine at position 29, is a substitution of Gly at position 192 for arginine (see WO95' page 6, lines 11-19).

(Instant claims 17, 28, 30, 32-34, 37, 38, 41-42) The compositions disclosed are for stimulating an immune response (see page 12, lines 1-19), the method comprising the step of administering the composition (see page 12, line 9; page 8, line 36-37).

(Instant claim 43) The method of preparing an antigenic composition comprises the step of:

Combining (admixture (seeWO95, page 6, lines 34-36) an antigen together with the mutant holotoxin in an adjuvanting amount (see WO95', page 18, claims 4-15).

The reference anticipates the instantly claimed invention as now claimed.

6. Claims 1, 2, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Glineur et al (1994).

Glineur et al disclose an antigenic composition that comprises a mutant holotoxin of cholera toxin referred as CTX-CRM-E29Δ. The mutant holotoxin has a tyrosine substituted at position 29, see Figure 2, frame B, line labeled CTX A E29Δ. The antigenic composition was recombinantly expressed in Vibrio cholerae 569B-NT, in association with a coding sequence for ampicillin resistance (see Figure 3 "amp", and "CTA", "CTB", and page 4180, col. 2, paragraph 1). Therefore the antigenic composition comprise a mutant cholera holotoxin with tyrosine substituted at position 29, the amino acid not being either glutamic acid or aspartic acid, and was in combination with at least two additional antigens, a 27 and 12 kDa antigen (see page 4180, col. 1, Figure 4, page 4181, lane labeled "E29Δ") as well as was in combination with all of the antigen produced by the recombinant host cell Vibrio cholerae 569B-NT upon expression. The culture medium is a type of diluent or carrier (see page 4180, col. 2 "CTX-CRM"). The reference inherently anticipates the instantly claimed invention as now claimed.

Conclusion

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

8. Feil et al is cited to show site directed mutagenesis of positions 47-53 of heat labile enterotoxin

9. Gu et al (US Pat. 6,685,949) is cited to show the utilization of a CRM molecule as a carrier for a detoxified lipopolysaccharide in a method of inducing an immune response.

10. Vadheim et al (1994) disclose a composition that comprises a mutant recombinant cholera toxin with a methionine at position 29, due to the deletion of amino acids 6-13, thus substituting the methionine at position 37 for the glutamic acid at position 29. New position 29 after deletion of amino acids 6-13 in subunit A, resulted in the substitution of methionine at position 29.

11.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
September 30, 2004

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